CASE REPORT

Rarity revisited: cryptococcal peritonitis

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SUMMARY

Cryptococcal peritonitis is a rare disease. Although the respiratory tract is considered to be the usual port of entry for the organism, the gastrointestinal tract can also serve as the potential site of entry. Here, we present a case of cryptococcal peritonitis that developed in an HIV-negative patient with underlying liver cirrhosis. We reviewed the literature and a total of 61 cases of cryptococcal peritonitis were identified. Liver cirrhosis, HIV/AIDS and end-stage renal disease on continuous ambulatory peritoneal dialysis were the major risk factors for developing cryptococcal peritonitis.

BACKGROUND

Cryptococcal peritonitis is an uncommon infection. Although the respiratory tract is the usual port of entry for the organism, the gastrointestinal (GI) tract can also serve as a potential site of entry when the organism is ingested or via direct blood stream inoculation following upper GI bleeding.^{1 2}

Here, we present a case of cryptococcal peritonitis that presented with increased abdominal distension and generalised fatigue. Abdominal paracentesis was performed and the patient was started on empiric treatment for suspected spontaneous bacterial peritonitis (SBP). However, the culture of ascitic fluid grew *Cryptococcal neoformans*. This patient presentation warrants the fact that the physicians should have a broad perspective in mind when dealing with patients who present with typical symptoms that might be pointing towards an obvious pathological process. However, the causative agent can be atypical, as it was evident in this case.

CASE PRESENTATION

A 60-year-old man, with a medical history of liver cirrhosis secondary to hepatitis B and hepatitis C, presented with increased abdominal distension and fatigue.

In the preceding 6 months, he had multiple admissions for treatment of hepatic encephalopathy and for banding of oesophageal varices. His HIV status was known to be negative.

On physical examination vital signs were stable. The abdomen was distended with shifting dullness to percussion and normal bowel sounds but without tenderness or guarding. His neurological examination was grossly normal. During the hospitalisation, the patient had nausea, diffuse abdominal discomfort and subsequently his mental status began to deteriorate.

INVESTIGATIONS

Full blood count revealed haemoglobin of 10.5 g/dL, white blood cell (WBC) count of 8600/mm³ and

platelets of 53 000/mm³. The electrolytes were all within normal range. Liver function testing showed aspartate transaminase of 69 U/L, alanine transaminase of 35 U/L, alkaline phosphatase of 107 IU/L and total bilirubin of 1.9 mg/dL. Prothrombin time was 21 s, partial thromboplastin time was 38 s and the international normalized ratio was 2. Chest X-ray showed small bilateral pleural effusions, with underlying atelectasis. An ultrasound-guided paracentesis was performed and 2 L of cloudy, yellow ascitic fluid was removed. Ascitic fluid showed 300/mm³ RBCs, 1250/mm³ WBCs with 90% lymphocytes, total proteins of 782 mg/dL (serum total proteins: 7.6 g/dL), albumin of 272 mg/dL (serum albumin: 2.3 g/dL) and a negative Gram stain. Within few days the patient's ascitic fluid culture grew *Cryptococcus neoformans*.

Upon deterioration of the patient's mental status, he underwent CT of the head which revealed no acute intracranial abnormality and a lumbar puncture was performed. The opening pressure was about 200 mm H₂O. Cerebrospinal fluid (CSF) analysis showed 214/mm³ WBCs (95% lymphocytes), 125 mg/dL proteins, 5 mg/dL glucose and 121 mEq/L chloride. CSF cryptococcal antigen by latex agglutination test (LAT) was positive. Tests to identify bacterial pathogens, other fungi and viruses were negative. Furthermore, blood cryptococcal antigen by LAT was positive as well. All the procedures were performed in complete aseptic conditions to avoid contamination.

DIFFERENTIAL DIAGNOSIS

The initial concern was of possible SBP complicated with hepatic encephalopathy. Initially, the patient was started empirically on ceftriaxone for suspected SBP. He was started on lactulose and rifaximin for treatment of suspected hepatic encephalopathy as well.

The patient had prior presentations with hepatic encephalopathy, which were associated with episodes of GI bleeding and responded well to medical therapy with complete resolution of encephalopathy, but this time the encephalopathy persisted despite medical therapy targeting hepatic encephalopathy. The ascitic fluid culture confirmed cryptococcal peritonitis and subsequently the lumbar puncture confirmed cryptococcal meningitis as a cause of his change of mental status.

TREATMENT

Treatment was started with amphotericin B and fluocytosine, but shortly the patient developed acute renal failure and the antifungal therapy was switched to fluconazole.

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Figure 1 Underlying disease in patients with cryptococcal peritonitis.

OUTCOME AND FOLLOW-UP

The patient's condition deteriorated over a week with hypotension that required treatment in the intensive care unit. The patient and his family elected to undergo home hospice care. Two weeks later, the patient had haematemesis with rapid deterioration of his condition and he died.

DISCUSSION

The genus *Cryptococcus* includes almost 40 species of which *C. neoformans* and *Cryptococcus gattii* are considered truly pathogenic in humans.³ Although other cryptococcal species rarely cause true infections, both *Cryptococcus curvatus* and *Cryptococcus laurentii* were described as a cause of peritonitis associated with gastric lymphoma and peritoneal dialysis, respectively.³⁻⁴ Of these pathogenic strains in humans, *C. neoformans*, which is encapsulated yeast, is mainly pathogenic in immunocompromised patients.

Cryptococcal organisms can be identified on cytology as narrow-based budding yeasts surrounded by a polysaccharide capsule. Different *C. neoformans* serotypes are based on the antigens present on the capsule. The capsule is periodic acid-Schiff positive that additionally stains strongly with mucicarmine stain. Also, the capsule can be readily demonstrated by the use of India ink stain.²⁻⁵⁻⁶ The Fontana-Masson stain can reveal the melanin contained in the yeast cell wall and it can be useful in some cases with poorly encapsulated *Cryptococci*.⁷ The major virulence

factors for *C. neoformans* are the antiphagocytic polysaccharide capsule, phenol oxidase enzyme that offers an antioxidant protective effect via catalysing melanin production and the temperature tolerance exhibited by the organism.⁸

Cryptococcal infections range from pulmonary involvement to disseminated disease that frequently involves central nervous system. However, cryptococcal peritonitis is a rare disease with a total of 61 cases reported between 1951 and 2012.¹⁻⁶⁻⁹⁻⁵⁴

Among all these cases, the mean age was 45 years and the ages ranged from 13 to 64 years. Underlying pathologies included cirrhosis in 45.9%, chronic kidney disease on continuous ambulatory peritoneal dialysis in 24.60% and HIV/AIDS in 19.7% (figure 1).

In these patients, the diagnosis of cryptococcal peritonitis was established by paracentesis and analysis of the peritoneal fluid. Along with the evidence of cryptococcal infection in the peritoneal fluid, positive specimens were also found in blood (36.10%), CSF (16.40%) and urine (8.20%). Other biological specimens also revealed the presence of cryptococcus, although their frequency was low (figure 2). Of all the patients whose outcome could be determined, 41% died (figure 3). Analysing the current data present on cryptococcal peritonitis suggests that the predisposing factors for this rare disease are similar to those seen in spontaneous bacterial peritonitis.²⁵

Patients who have hepatic disease are already at increased risk of infections due to impaired phagocytic function of leucocytes,

Figure 2 Specimen yielding *Cryptococcus*. NA, not available.

Figure 3 Outcome of cryptococcal peritonitis. NA, not available.

hypocomplementaemia, increased use of antibiotics with possible fungal overgrowth, the necessity to carry out invasive procedures that may cause direct inoculation of the organism and due to GI bleeding which can cause translocation of the organism into the blood stream from GI sites.^{2 6 10 11} All these factors act in concert to make the patient more vulnerable to cryptococcal infection.⁵

Patients with cryptococcal peritonitis usually have initial symptoms of abdominal pain, fever, increased abdominal girth besides non-specific signs and symptoms upon presentation which makes the diagnosis challenging.^{2 9 13 14} However, with the assistance of ascitic fluid cytology and simultaneous India ink preparation, the patient can be readily evaluated for the possibility of cryptococcal peritonitis. Although culture is the gold standard for diagnosis of cryptococcal infection, the diagnosis of cryptococcal peritonitis can be delayed if cytological analysis of the ascitic fluid is not employed.

In conclusion, despite being a rarity, cryptococcal infection should be considered in the differential diagnosis whenever evaluating a patient with an advanced liver disease and possible peritonitis, especially with concomitant immunocompromised state.

Learning points

- An uncommon causative organism can be missed if the patient presents with manifestations of a common pathology.
- A thorough workup of the patient is essential when the presenting symptoms are not responding to the routine treatment employed.
- Cryptococcal peritonitis can mimic spontaneous bacterial peritonitis, yet discerning the organism can be a diagnostic challenge and cannot be always determined, particularly if the suspicion is not broad-based in the initial workup.
- Although an uncommon cause of peritonitis, fungal peritonitis in general needs to be in the list of differential diagnoses when a patient with relevant history and comorbid conditions presents to the healthcare facility, especially when the routine therapeutic measures are not proving to be effective.

Patient consent Obtained.

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